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Original Research Article

A Research Study on the Characteristics and Outcome of Cardiorenal Syndrome in Patients with Heart Failure

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Abstract:

Aim & Objectives: This study aims to evaluate the frequency, predictors, and consequences of Cardiorenal syndrome (CRS) among patients admitted to tertiary care hospital medical wards with heart failure (HF).

Material & Methods: There was a cross-sectional design used in the research. Over the course of 15 months, patients who fulfilled the inclusion criteria and were at least 18 years old were recruited one at a time. Along with the necessary baseline blood tests—blood profile, complete blood count, urine analysis, estimated glomerular filtration rate (eGFR), electrocardiography (ECG), echocardiography, and renal ultrasound scan—a thorough medical history and physical examination were performed. In patients with proteinuria, the urine protein creatinine ratio was assessed. Serum creatinine, urea, and electrolyte levels were measured at the time of first presentation. Afterwards, over the course of heart failure therapy, same measures were conducted once more. Heart failure and CRS were accurately described and categorised using appropriate standards. Statistical analysis carried out using the SPSS software.

Results: Of the 100 patients analysed, the mean age was 50.64±13.4, with 62 males and 38 females. 53 of them acquired cardiorenal impairment, and 47 of them are in the group of patients with heart failure alone. 86.8% of the CRS group is older than 40 (p=0.04) and has a high frequency of diabetes, compared to 76% of the non-CRS group who do not smoke. A large proportion of those affected have type 1 CRS, and 72.5% of CRS cases fall into the moderate CRS category. Mortality can be predicted by serum urea >120 mg/dl and serum creatinine >1.91 mg/dl. Individuals identified as having CRS had noticeably higher death rates than those without the condition.

Conclusion: Significantly higher rates of CRS were seen in patients with heart failure. Age above 40 years old and NYHA class 4 were revealed to be independent predictors of CRS. Compared to patients without CRS, patients with CRS stay in the hospital for a much longer period of time. In a hospital context, the mortality rate for patients with CRS is noticeably higher. Serum urea and creatinine are important markers of mortality.

Keywords: Cardiorenal syndrome; Creatinine; GFR; Heart failure; Urea.

Introduction

Heart failure (HF) is becoming identified as a global public health concern that affects countries of different economic status. In places with low resources, the substantial burden of high HF and the need for resource-intensive therapies can lead to health system crises. [1] According to the INDUS study, there are approximately 1.2 cases of the ailment for every 1000 people in India. Heart failure has a 7.2% one-year mortality rate and a 31.9% one-year hospitalisation rate in patients with chronic heart failure following its beginning. However, these percentages increase to 17.4% and 43.9%, respectively, among individuals brought to the hospital with acute heart failure. The number of people with heart failure worldwide has increased to over 23 million. [2] A medical disease known as cardiorenal syndrome (CRS) causes abrupt or chronic dysfunctions in the heart and kidneys,

which in turn cause dysfunctions in another organ. Alterations in neuro-hormonal biomarkers and pro-inflammatory molecular fingerprints peculiar to its clinical features, as well as the blood flow dynamics among the failing heart and the kidneys and vice versa. [3] The sympathetic nervous system, inflammation, renin-angiotensin-aldosterone system (RAAS) alterations, and a disparity amongst nitric oxide (NO) as well as reactive oxygen species (ROS) are all associated with the development of cardiorenal syndrome. These elements function as the links that connect the renal and cardiovascular systems.[2] Renal perfusion pressure decreases with heart failure, which causes the blood arteries that supply the kidneys with blood to constrict (afferent arterioles). As a result, the glomerular filtration rate (GFR) and renal blood flow are further reduced. The consequences of heart failure (HF) are more severe because catecholamines are released more often and eliminated less frequently. [4]

Patients with heart failure (HF) frequently experience renal impairment (RI), and between 20% and 40% of patients hospitalised to hospitals for acute heart failure syndromes (AHFS) additionally experience renal impairment (RI) at the same time. [5] Renal impairment, defined as an increase in serum creatinine of at least 25% or values that are equal to or higher than 2 mg/dl, was previously seen to be common in patients undergoing intense treatment for heart failure.[6] Patients with progressive renal failure increasingly see cardiovascular conditions as the main killer.[7] Concurrent kidney disorders and heart failure are becoming recognised as distinct risk factors that cause disease and mortality.[8] The management of people with heart failure and the forecast of their prognosis are significantly affected by the convergence of each of these variables. [9] The risk of cardiovascular disease is greatly impacted by even a minor impairment in kidney function, as evidenced by an increase in blood creatinine or a decrease in estimated glomerular filtration rate (GFR).[10] Studies show that for every 1 ml/min drop in creatinine clearance, patients' mortality increases by 1%. Furthermore, people who experience a little decline in renal function run the same cardiovascular risk as those who have diabetes mellitus.[11,12] Regardless of standardised indicators of heart failure severity, renal insufficiency is associated with unfavourable outcomes and is not only a marker of advanced cardiac disease but also a direct cause of morbidity and mortality in persons with HF. Studies have shown that hospitalised patients with acute heart failure syndrome (AHFS) have increased risks of morbidity and mortality when they had baseline renal impairment (RI). [5–15] The greatest independent predictor of readmission for any cause was found to be a serum creatinine level more than 2.5 mg/dL at the time of release, according to an extensive analysis of data from 1,129 individuals. The range [5,16] Data from 541 people were used for a multivariate Cox regression analysis, which showed a strong correlation between rising quartiles of xv Blood urea nitrogen (BUN) and all-cause death. [5,17] According to an analysis of data from the SOLVD trial, patients who had both left ventricular systolic dysfunction (LVSD) and renal dysfunction were more likely than those who had both normal renal function and LVSD to experience more severe heart failure symptoms, as indicated by their higher NYHA Class. [19] A research by HR Shah et al. looked at the clinical traits and results of people with CRS in North India. As a result, little is known about the incidence of various kinds of CRS, the factors that influence them, their effects on health and mortality rates in Central India, and their contributing factors. In addition, primary care physicians treat an increasing number of cardiovascular diseases that cause heart failure and kidney problems in the rural population. The range [4,9] Thus, the purpose of this study was to ascertain the prevalence, classifications, and outcomes (i.e., duration of hospital stay and death) of people with CRS. Moreover, to identify the risk factors associated with death in people with CRS. The incidence and death rates related to CRS can be lowered with prompt diagnosis of certain risk factors.

Aims and Objectives:

The study's goals were to determine the frequency and effects of CRS in patients admitted to the outpatient facility with heart failure (HF) as well as the following:

1. To determine the traits that may be predictive of and etiologically contributing to the emergence of chronic respiratory symptoms (CRS) in heart failure (HF) hospitalized patients.
2. To evaluate the duration of hospital stay and death rate of CRS patients admitted for heart failure (HF). The study also attempts to determine the factors that lead to death in CRS patients who are hospitalised for heart failure.

Materials and Methods:

The study was conducted in the medical department of a medical college hospital. The design of the study is cross-sectional. Patients who met the Framingham criteria for heart failure and were hospitalised for at least 18 years were included in the research. The study did not include patients who refused to grant consent to take part in the experiment and were already getting regular dialysis therapy prior to enrolment. The institutional Ethical Committee approved the research, and each patient provided informed consent. The proclamation of HELSINKI was

adhered to. Patients who satisfied the requirements were added one after the other until the target sample size was attained.

A standardised Proforma was used to ask patients that had been suspected of having heart failure questions about their clinical history, anthropometric measurements, general and cardiovascular examinations, and demographic data. Serum creatinine [SCr], urea along with electrolytes [U/E/], blood sugar levels, serum uric acid, blood lipid levels, urine analysis, electrocardiogram (ECG), and echocardiography were among the diagnostic tests performed on the patients. When a person had protein in their urine during a urinalysis, the urinary protein-creatinine ratio was calculated to determine how much protein was eliminated in a 24-hour urine sample. Every person had a renal ultrasonography scan done.

The glomerular filtration rate (GFR) of Indian patients was predicted using the Cockcroft-Gault equation, that has been extensively tested and shown to reliably estimate GFR. [20–22] Serum creatinine [SCr], urea, & electrolyte levels [U/E] have been evaluated at the end of the therapy or on day seven. The modified Framingham Criteria were used to make the diagnosis of heart failure. [23] An estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m2 was used to diagnose renal damage in heart failure (cardiorenal syndrome). The range [4,9] The New York Heart Association (NYHA) functional class was used to assess the severity of clinical symptoms.[20]

Methodology:

A traditional mercury sphygmomanometer was used to measure the blood pressure in both the left and right arms. The arm with the highest measured blood pressure was measured and recorded. The weight was measured in kilogrammes utilising a weight-based scale with twelve lead surfaces, and the height was measured in metres using a stadiometer. The heart's electrical activity was recorded using an ECG. Using ECG equipment, the investigator recorded each participant who was enrolled. For each patient, the researcher performed transthoracic echocardiography. The measurements were performed utilising the leading-edge to leading-edge convention and simultaneous ECG recording, in compliance with the recommendations set out by the American Society of Echocardiography (ASE). [19]

An unbroken and continuous signal or transmission is referred to as continuous-wave. When there was a possibility of a valvular anomaly, the Doppler method was used to examine the valves. In patients with diastolic dysfunction, tissue Doppler imaging was utilised to differentiate among normal & pseudo-normal left ventricular filling. White blood cell counts and haemoglobin estimation were performed using an EDTA blood collection container. Following an 8–12 hour overnight fast, 10 ml of venous blood was drawn to evaluate lipid profiles (triglycerides, total cholesterol, low-density lipoprotein, HDL, and LDL) and fasting blood sugar (FBS).

An automated analyzer was used to measure the amounts of creatinine, urea, and electrolytes in the serum. All of the samples were analysed by the central lab.

Data Analysis:

Version 16.0 of the computerised statistical software package for social sciences, or SPSS, was used to construct, verify, and analyse the acquired data. Quantitative variables were described using the mean and standard deviation. Statistical significance was defined as a P value of less than 0.05.

Observation and Results:

One hundred patients in all who met the requirements for inclusion were examined. They had a male: female ratio of 1.6:1, with 62 (62%) males & 38 (38%) females. The patients ranged in age from 18 to 90 years, with a mean age of 50.641 ± 13.439.

Table 1: Baseline characteristics of patients

Variables	N
Age (years)	50.641±13.439
Gender Male	62
Female	38
Hypertension	57
Diabetes	49
Dyslipidemia	46
Smoking	37
Alcoholic	39
Hypothyroidism	16
Systolic dysfunction	51
Diastolic dysfunction	49
Clinical aetiology of HF Hypertensive heart disease	37
Dilated cardiomyopathy	35

Peripartum cardiomyopathy	10
Rheumatic heart disease	10
Ischemic heart disease	2
Cor-pulmonale	3
Systolic blood pressure (SBP) (mm Hg)	127.61±33.039
Diastolic blood pressure (DBP) (mm Hg)	74.729±10.891
Haemoglobin (Hb) (mg/dl)	10.459±1.901
Serum urea (mg/dl)	50.711±24.791
Serum creatinine (mg/dl)	2.101±3.099
eGFR (ml/min)	59.351±33.301
Total cholesterol (TC) (mg/dl)	193.79±57.791
Left ventricular ejection fraction (LVEF) (%)	44.89±11.801

Majority of patients have dyspnoea of grade 4. Compared to the group without CRS, those with CRS, 86.8% were above 40 years (86.8% vs. 69.6% p <0.04), had higher frequency diabetes (62.3% vs. 34.8% p= 0.0091) (Table-2).

Table 2: Comparison of the clinical characteristics and echocardiographic findings among the patients

Variables	Total	CRS present	CRS absent	P-value
	n=100	n=53	n=47	
Gender-Male	62	37	25	0.147
Female	38	16	22	
Age(years)	50.641±13.439	53.511±13.591	47.329±12.589	0.021
BMI	23.089±2.601	23.279±2.201	22.879±3.021	0.449
Hypertension	57	34	23	0.219
Diabetes	49	33	16	0.0091
Paroxysmal nocturnal dyspnoea (PND)	81	50	31	0.0011
Orthopnoea	80	50	30	0.0011
Jugular venous pressure (JVP)	76	45	31	0.0439
Cardiomegaly	83	49	34	0.0101
Third heart sound (S3)	75	47	28	0.0011
Systolic Dysfunction (SD)	51	24	27	0.3701
Diastolic Dysfunction (DD)	58	34	24	0.449
LVEF <50	72	37	35	0.338

Of the CRS group, 9.3% earned severe grades, 18.5% got moderate marks, and 72.2% had mild grades. 41 people (77.35%) with CRS diagnoses made up the bulk of those who suffer with the condition. Eight individuals (15.09%) had type II CRS, while the remaining four patients (7.5%) had type IV CRS. Type III and V CRS were not seen in any of the study subjects.

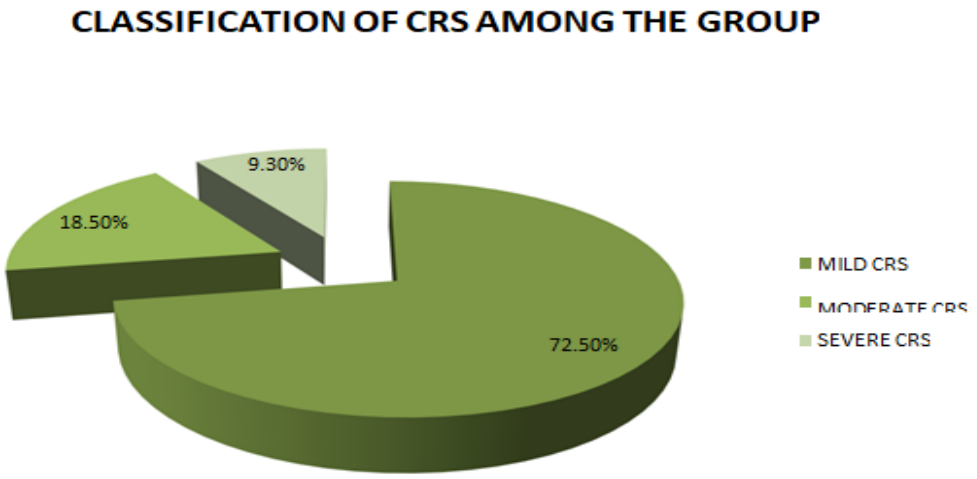

Figure 1:

CRS classification within the CRS group is shown in Figure -1. Severe: HF+eGFR <15mL/min/1.73m2 or dialysis; mild: HF+eGFR 30-59mL/min/1.73m2, moderate: HF+eGFR 15-

29mL/min/1.73m2,

The CRS 2 group had significantly greater average serum urea (59.51 mg/dl vs. 39.61 mg/dl, p=<0.0001) & creatinine (3.13 mg/dl vs. 1.01 mg/dl, p=<0.0001) than the group without CRS. On the other hand, Table 3 shows that the mean eGFR in the CRS group was considerably lower (34.99 ml/min versus 87.40 ml/min, p<0.0001).

Of the participants in the research, 75 people or 75% had proteinuria. Of the total patients, 33.33% of those with without CRS had proteinuria, whereas 66.66% of those with proteinuria had CRS. A p-value of 0.0171 indicated that there was a statistically significant difference.

Table 3: Comparison of the laboratory parameters among patients with & without CRS

Variables	CRS present	CRS absent	P-value
	Mean±SD	Mean±SD	
Hb (mg/dL)	10.324±1.741	10.614±2.101	0.4551
Total cholesterol (mg/dl)	191.681±64.129	196.141±50.089	0.7029
eGFR (ml/min)	34.989±11.981	87.402±27.361	<0.0001
Urea (mg/dl)	59.511±26.449	39.611±17.682	<0.0001
SCr (mg/dl)	3.131±3.749	1.012±1.231	<0.0001

Table 4: Comparison of clinical variables among patients with and without cardiorenal syndrome

Variables	CRS present	CRS absent	P-value
	n=53	n=47	
Age (>40years)	46	32	0.0401
SBP >160mmHg	15	5	0.0399
Diabetes	33	16	0.0089
NYHA IV	33	15	0.0081
Anaemia	24	17	0.4211

Table 5: Mortality and duration of hospital stay

Variables	Total patients	CRS present	CRS absent	P-value
	n=100	n=53	n=47	
Death	35	31	4	<0.0001
Duration of stay (days)	9.411±7.089	10.419±3.701	8.259±9.511	<0.0001

The patient outcomes (death and length of hospital stay) are displayed in Table 5. 35 (35%) of the 100 participants passed away. 31 people (58.5%) in the CRS group and 4 people (8.7%) in the non-CRS group passed away (p value <0.0001), indicating a considerably greater death rate in the CRS group. The CRS group's mean hospital stay lasted 10.42 ± 3.70 days, while the non-CRS group's mean stay was 8.26 ± 9.55 days (P value<0.0001).A comparison of the results for the CRS and non-CRS groups.

Table 6: Comparison of Deceased and Survivors of CRS

Variables	Deceased	Survivors	P-value
	n=31	n=22	
NYHA class IV (%)	20 (64.51)	11 (50)	0.0091
DM	722.8	418.18	0.901
SBP <160mmHg	15 (48.38)	18 (90.6)	0.001
DBP <60mmHg	4 (11.4)	10 (15.6)	0.759
SCr >1.91mg/dl	20 (64.51)	10 (45.45)	0.0011
Urea >120mg/dl	13 (41.93)	5 (22.72)	0.0011
eGFR <53ml/min	31 (100)	19 (86.36)	0.0449
Cholesterol >200mg/dl	14 (40.0%)	28 (43.8)	0.8301

A juxtaposition of laboratory and clinical results between CRS survivors and those who died is shown in Table 6.

Patients with SCr levels of ≥1.91 mg/dl, urea levels of >120 mg/dl, eGFR levels of <53 ml/min, and NYHA class IV included a significantly higher proportion of the expired (p=0.0011, 0.0011, 0.0449, and 0.0091, respectively). Conversely, a greater proportion of participants with systolic blood pressure (SBP) values below 160 mmHg (p=0.001) was found among the survivors.

Discussion:

53.5% of the research participants had the disorder. The current study's prevalence rate is somewhat higher than previous reports from numerous local research studies on the incidence of renal damage in heart failure patients. [7,8] In the studies, the

incidence of kidney damage in individuals admitted for heart failure ranged from 7% to 50%. Differences in the research technique and the study participants' demographic makeup might be the cause of the contradictory results. However, a number of earlier studies have shown that CRS occurs rather often. [22–24] A specific study revealed that a moderate degree of cardiorenal syndrome (CRS) was present in 60% of individuals given the diagnosis of acute decompensate heart failure (ADHF). [24] The mean age of the participants in this research was 50.64 ± 13.44 years, which is rather young. This discovery is consistent with the results of a previous study that was carried out on heart failure patients at the study site and another study that involved patients from western Odisha, in the western region of Nigeria. Participants in both trials were 45.531 ± 8.611 years old on average.[7] Nevertheless, these results are at odds with the greater average ages discovered in studies carried out in Maharashtra (71.358± 6.481 years), the USA (61.01 ± 18.01 years), and Europe (71.31 ± 12.71 years).The age difference might be, at least partially, explained by the fact that the Indian population has an earlier beginning of some heart failure-related conditions, such as peripartum cardiomyopathy & rheumatic heart disease. [26] The study revealed that among the persons with heart failure who fell into NYHA class IV and were older than 40, there was a correlation with CRS. Within their cohort, McAliter et al. found that 39% of those diagnosed in NYHA class IV & 31% of participants in NYHA class III who had heart failure symptoms had a notable degree of renal impairment.[13] In contrast to the rates shown in other studies, the mortality rate of 58.5% among CRS patients seen in this study was much higher. [17] The outcome of the clinical study of HR Shah et al.'s Cardiorenal research revealed a 16% overall mortality rate. [4] The majority of the patients in our research had severe heart failure, that may explain the higher death rates found in earlier studies. Compared to patients without CRS, individuals with CRS had a substantially longer hospital stay (10.421±3.704 versus 8.261±9.552, p value-0.0001). According to a study done in the United States of America, people with heart failure over 65 who experienced acute renal impairment had a two2% greater chance of dying and a thrice longer hospital stay. However, there was no discernible difference in the duration of hospitalisation between patients who had increased renal dysfunction and those who did not, according to a study done in Nigeria on the aggravation of renal malfunction in heart failure patients.[8] In this study, the only markers of mortality were a blood urea value more than 120 mg/dl and a creatinine concentration in the serum of 1.9 mg/dl or higher. In individuals with CRS, renal dysfunction assessments have been found to be more powerful predictors of death than LV dysfunction markers (LVEF and NYHA). [11,18] Blood creatinine levels as well as mortality in heart failure patients were found to be significantly correlated by HR Shah et al.[4] In the outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbation of Chronic Heart Failure investigation, elevated serum creatinine (SCr) and urea levels were found to be significant and independent predictors of mortality or re-hospitalization. [27] After controlling for other variables, a research that examined 1004 consecutive patients with heart failure who received treatment to 11 different hospitals revealed a 7.5-fold increased risk of mortality during the hospital stay for patients with declining renal function. [28]

Conclusion:

Heart failure patients had a high incidence of CRS. Age above 40 years old and NYHA class IV were revealed to be independent predictors of CRS. Compared to patients without CRS, patients with CRS stay in the hospital for a much longer period of time. In hospital settings, the death rate is much higher for those with CRS. Measurements of renal function, particularly a serum creatinine (SCr) level more than 1.91 mg/dl along with a urea level greater than 120 mg/dl, were found to be the predictors of mortality. It was difficult for some patients to determine which primary organ—the heart or the kidneys—was failing, which may have affected how CRS was divided into different categories. The prevalence of CRS may have been affected by the removal of certain populations of patients with heart failure, especially those who attended outpatient clinics.

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